

U.S.S.N. 10/792,302
Filed: March 3, 2004
AMENDMENT AND RESPONSE TO OFFICE ACTION

Remarks

Amendments to the Claims

The undersigned and inventors greatly appreciated the opportunity to speak on April 11, 2005, with the examiner and his supervisor regarding this case, and the very helpful suggestions and inciteful questions.

As discussed during the interview, applicants are not isolating a single clone but a population of multipotent mammalian cells isolated from tissue or a tissue derived cell suspension. These are not stem cells (see page 24, lines 11-18). Therefore the claims have been amended to recite these features, as suggested by the examiner's supervisor. Support for multipotent cells is found, for example, at page 2, line 22. Isolation from tissue is found at page 2, bottom of page 4, top of page 7, and in the examples. Although there is no reason to believe these cell populations can only be isolated from mammals, the claims have been limited to mammalian cells since all of the examples relate to mammals – rats, sheep, humans. Support is found for the term "mammalian" at page 37, line 8.

The claims have been amended to define the claimed subject matter as a method for isolating this population of cells. As was emphasized during the interview by Dr. Vacanti, the method for separating spore-like cells from differentiated cells, includes exposing a mixture of the cells to conditions that kill the differentiated cells but not the spore-like cells. Independent claim 1 was previously amended to define the conditions that kill normal

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differentiated cells but not the spore-like cells. The dependent claims now more specifically also define the features of the cells, such as the amount of nuclear material, the size, and the lack of differentiation. These conditions are found at page 6, lines 12-29; page 15, lines 19-23; page 18, lines 1-25 (conditions to kill differentiated cells), page 7, lines 7-12 (separation by filtration); page 14, lines 20-28 (spore like cells are multipotent); page 14, line 29 to page 15, line 2; page 15, lines 15-18; page 16, line 29 to page 17, line 17; see also Figures 1 and 2 (size, amount of nucleus).

Rejections under 35 U.S.C. 112

Claims 1-27 were rejected under 35 U.S.C. 112 as failing to comply with the written description requirement and definiteness. These rejections are respectfully traversed if applied to the amended claims.

The principal basis of the rejection is that the spore-like cells are not clearly defined. It is believed this aspect of the rejection has been mooted by defining the method as one which isolates a multipotent cell population using conditions that are used to kill the differentiated cells but not the spore-like cells, and defining the distinguishing characteristic separating the two types of cell as that multi- or pluripotent spore-like cells remain viable when exposed to the specific conditions, and the differentiated cells do not, as well as by describing in the specification the size, nuclear structure, and phenotypic characteristics of the spore-like cells, including actual SEMs of these cells from different tissues of origin (see examples 11 and 12, page 38).

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The examples clearly demonstrate that the claimed method was actually reduced to practice with a variety of different means of killing the differentiated cells but not the spore-like cells, and that the cells could then be separated. This fully complies with the written description requirement. Indeed, the specification not only shows that the applicants were in possession of the claimed method, but had reduced it to practice on multiple occasions.

Example 1 demonstrates that spore-like cells were isolated from human blood (first species, first cell type) using repeated passaging in cell culture.

Example 2 demonstrates that spore-like cells were isolated from rat (species 2) skin (second cell type). The technique used for all of examples 2-10 was size separation (passaging through smaller and smaller bore pipets) followed by passaging in cell culture.

Example 3 demonstrates that spore-like cells were isolated from rat heart (third cell type).

Example 4 demonstrates that spore-like cells were isolated from rat intestine (fourth cell type).

Example 5 demonstrates that spore-like cells were isolated from rat bladder (fifth cell type) 2.

Example 6 demonstrates that spore-like cells were isolated from rat kidney (sixth cell type).

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Example 7 demonstrates that spore-like cells were isolated from rat liver (seventh cell type).

Example 8 demonstrates that spore-like cells were isolated from sheep (third species) and rat lungs (eight cell type).

Example 9 demonstrates that spore-like cells were isolated from rat adrenal glands (ninth cell type).

Example 10 demonstrates that spore-like cells were isolated from human and rat pancreas (tenth cell type).

Examples 13 and 14 demonstrates that spore-like cells were isolated from rat lung, liver, fascia, and spinal cord (four tissues, including two additional cell types) using enzyme digestion, storage in the refrigerator or freezer without supplemental oxygen (second technique) and passage through smaller and smaller pipets.

Example 15 demonstrates that spore-like cells were isolated from rat lung, liver, fascia, and spinal cord by heating to 85°C (third technique). Trypan blue uptake was used to differentiate the viable from the dead cells.

Example 17 demonstrates isolation of spore-like cells from human blood that had been stored frozen for eight years and then were repeatedly frozen and unfrozen, and separated by passage through filters and pasteur pipets.

In summary, spore-like cell populations were isolated using three completely different techniques: size separation and passage through cell

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culture; storage in the substantial absence of oxygen; and heating. Spore-like cells were isolated from three different species: human, rat and sheep.


Finally, spore-like cells were isolated from twelve different cell types: blood, lung, liver, adrenal gland, fascia, spinal cord, skin, pancreas, kidney, bladder, intestine, and heart. The cells were characterized functionally, histologically, by SEM, and by phenotype.

The claims now provide a simple, easy and definitive means for practicing the method: one simply performs one or more of the recited means for killing differentiated cells but not spore-like cells, and then retains the viable cells, which are by definition the spore-like cells.

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Allowance of claims 1-27, as amended, is respectfully solicited.

Respectfully submitted,



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